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Sensitivity of rapid antigen tests for COVID-19 during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs: Retrospective observational study

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Abstract

Objectives

Rapid antigen tests have been used to prevent the spread of the coronavirus disease 2019 (COVID-19); however, there have been concerns about their decreased sensitivity to the Omicron variant. In this study, we compared the sensitivity and specificity of the rapid antigen and the polymerase chain reaction (PCR) tests among the players and staff members of the Japan Professional Football League and clubs. Furthermore, we evaluated the relationship between the sensitivity and the duration from the onset of the symptoms to testing, the manufacturer of the rapid antigen test kits, and the sample type of the PCR test.

Design

This was a retrospective observational study.

Methods

We used 656 results from both the rapid antigen and PCR tests for COVID-19 using the samples collected on the same day from January 12 to March 2, 2022, during the Omicron variant outbreak in Japan.

Results

The sensitivity of the rapid antigen test compared with the PCR test was 0.63 (95% confidence interval: 0.54–0.72) and the specificity was 0.998 (0.995–1.000). There were no significant associations between the sensitivity and the duration from the onset of the symptoms to testing (including asymptomatic cases in the category), vaccination status, manufacturer of the rapid antigen

test kit or sample type of PCR ($P > 0.05$) with small effect sizes (Cramer's V or φ: ≤ 0.22).

Conclusions

Even during the Omicron outbreak, the sensitivity of the rapid antigen tests did not depend on the duration from the onset of the symptoms to testing.

Strengths and limitations of this study

- We assessed the sensitivity of the rapid antigen test against the PCR test for COVID-19 during the Omicron variant outbreak among the players and staff of the Japan Professional Football League and clubs.
- We found that the sensitivity was 0.63 (95% confidence interval: 0.54–0.72) and independent of the duration from the onset of the symptoms to testing.
- The rapid antigen test can be performed more frequently than the PCR test under the same financial resources, and is expected to be highly effective in controlling infection among professional sports populations.
- Since the participants were professional sport players and staff members, cautions are required in applying the findings of this study in general populations.

INTRODUCTION

To prevent the spread of the coronavirus disease 2019 (COVID-19), active testing has been used to identify and isolate infected individuals, especially in populations at high risk of infections [1]. Among the various testing methods including the reverse transcription-polymerase chain reaction (PCR) test, antigen quantitative test, and rapid antigen test, the rapid antigen test is less sensitive, but it has the advantage of being inexpensive and providing prompt test results [2]. In particular, highly-frequent routine testing using rapid antigen test kits is more promising in reducing the spread of infection than highly-sensitive, but low-frequent testing [3]. It has been noted; however, that the sensitivity of the rapid antigen tests may be lower in Omicron variants than in previous variants [4 5]. In addition, the sensitivity of the rapid antigen tests may be particularly lower during the few days after infection (preprint)[6]. Since the testing and identification of infected individuals is more effective in controlling the spread of infection during the short period between infection and testing, there is concern that the lower sensitivity of the rapid antigen test during the short period after infection, may reduce the effectiveness of the testing system in the population. However, contrary to this, a previous study reported no large differences in the analytical sensitivity of the rapid antigen test in a comparison between representative Delta and Omicron isolates, using ten test kits [7]. In another case study with human participants, there was also no difference in the sensitivity of the rapid antigen test between the Delta and Omicron variants (preprint) [8]. Since both rapid antigen tests and other tests (e.g. PCR tests) must be performed using the samples collected on the same day from the same individuals to evaluate the sensitivity of the rapid antigen tests, studies based on human participants have been

limited [9] and these findings were not sufficient.

The Japan Professional Football League, a professional league of the most popular sports in Japan, collected the results of rapid antigen and PCR tests for COVID-19 among players and staff members in order to maintain and promote its activities [10]. If the rapid antigen test was positive, the subject was required to remain at home until the results of the PCR test or the physician's diagnosis are obtained. If the PCR test was positive, the subject had to visit a medical institution. Since January 2022, rapid antigen tests were conducted twice a week on a regular basis, and moreover, additional PCR tests were often conducted on players and staff members in the clubs where infected individuals were identified. Consequently, from January 12 to March 2, 2022, during the period when the Omicron variants emerged in Japan, the number of cases in which both rapid antigen and PCR tests were performed on the same day exceeded 650, which made it possible to evaluate the sensitivity of the rapid antigen and PCR tests.

In this study, we compared the results between the rapid antigen and PCR tests for COVID-19 among the players and staff of the Japan Professional Football League and clubs to determine the sensitivity and specificity of the rapid antigen and PCR tests. We then assessed the relationships between the sensitivity and the duration from the onset of the symptoms to testing, the manufacturers of the rapid antigen test kit, or the sample types of the PCR tests.

METHODS

Ethics

This study was conducted with the approval of the Ethics Review Committee of the Institute of Medical Science, University of Tokyo (approval number 2022-1-0421). Testing was not conducted originally for research purposes and the Japan Professional Football League does not have personal information on all the results. Therefore, information about this study was disclosed on the websites of the Institute of Medical Science of the University of Tokyo and the Japan Professional Football League to provide participants with the opportunity to opt out of the study. The person in charge of each club also provided information about the study to potential participants (players and staff members).

Participants

This study was a retrospective observational study. We obtained the test results from January 12, to March 2, 2022. This was the period of the Omicron variant outbreaks in Japan (98.92% on February 7, 2022) [11]. The data included a total of 656 cases in which both rapid antigen and PCR tests were performed using the samples collected on the same date from players and staff members of the Japan Professional Football League and clubs. In total, Japan Professional Football League and clubs had 1,759 players and 1,864 staff members (as of February, 2022). Each club has its own testing manager and physician. Among 58 clubs from J1 (the highest grade) to J3 (the lowest grade) in Japan Professional Football League, 23 clubs were included in this study. Since personal information on the participants was not available, the breakdown of the number of players and staff members in 656 cases was unknown. In the process of collecting the test results from players and staff members, some

of the cases in which both tests were negative may not have been available: i.e., the number of cases reported in this study in which both tests were negative may have been smaller than the actual number.

Survey items

The information used in this study included the positivity or negativity of each test, the presence or absence of symptoms, duration between the onset of symptoms and testing, vaccination status (i.e., whether the participants were vaccinated: at least once, none, or unknown), the manufacturer of the rapid antigen test kit, the sample types of the PCR test (i.e., "saliva," "nasal swab," or "either or other"), and the type of test ("regular test," defined by the use of a routine rapid antigen test twice a week by the Japan Professional Football League or a "voluntary test" other than a routine test). The onset of symptoms was based on the tally by the Japan Professional Football League, which comprised the individuals' self-reported information that their health condition was different from usual (e.g., fever, sore throat). The date of the onset of symptoms represented the date when the symptom developed. Asymptomatic cases represented those who did not exhibited symptoms up to the time of testing and after.

The rapid antigen test was performed using nasal swab samples, and the kits were the Abbott Panbio™ COVID-19 Antigen Rapid Test or the Roche SARS-CoV-2 Rapid Antigen Test. The sample types of the PCR test were saliva or a nasal swab. Both samples were generally self-collected by the participants themselves except some rare cases of the collection by the testing managers or physicians. The samples for the rapid antigen and PCR tests were collected separately. These samples

collected from the participants were not pooled and were analyzed separately. The players and staff members of the Japan Professional Football League and the clubs received lectures from their physicians on how to collect samples. Each club sent their samples to a medical or measuring laboratory for PCR testing. A Ct (threshold cycle) value of < 40 was considered as positive. PCR test results were notified from two hours to the next day after sample collection. Other details of the analytical information of the PCR tests were not available. Since information on the manufacturer of the rapid antigen test kits and the sample types of PCR was not available on an individual basis, we instead matched the individuals and their club using the information that was obtained from a survey of how each club conducted testing during the period. The clubs determined whether the manufacturer of the rapid antigen test kit was Abbott, Roche, or either, and whether the sample types of PCR were saliva, nasal swab, either, or other. The results (positivity or negativity) of the rapid antigen test among each of the 103 PCR-positive cases according to the duration from the onset of the symptoms to testing (including asymptomatic cases in the category) were reported on the website of the Japan Professional Football League [12].

Patient and public involvement

Patients and the public were not involved in the design, or conduct. The information about this study was disclosed on the websites of the Institute of Medical Science of the University of Tokyo and the Japan Professional Football League.

Statistical analysis

In this study, the sensitivity and specificity of the rapid antigen test against PCR test were first calculated by comparing the results (positivity or negativity) between both tests. Next, among the cases with positive PCR results, the chi-square test or Fisher's exact test was performed to investigate the associations between the results of the rapid antigen test (positivity or negativity) and the duration from the onset of the symptoms to testing (including asymptomatic cases in the category), vaccination status, manufacturer of the rapid antigen test kit, sample types of PCR, or test type. As an additional stratified analysis, only vaccinated individuals, those whose rapid antigen test kit manufacturer was Abbott, and those whose PCR sample type was saliva were used to examine the relationships between the rapid antigen test result (positivity or negativity) and the duration from the onset of the symptoms to testing (in categories asymptomatic included) using the chi-square test or Fisher's exact test. In this stratified analysis, −2 and −1 days were grouped together as one category for the duration from the onset of the symptoms to testing. Similarly, one and two days were combined into one category. IBM SPSS version 28 and R 4.2.0 [13] were used for the statistical analysis.

RESULTS

Of the 656 cases, 65 were positive for both the rapid antigen and PCR tests, 38 negative for the antigen tests and positive for the PCR test, one was positive for the rapid antigen test and negative for the PCR test, and 552 were negative for both (Table 1). The sensitivity of the rapid antigen tests compared with the PCR tests was 0.63 (95% confidence interval (CI): 0.54–0.72) and the specificity was 0.998

(95% CI: 0.995–1.000).

Table 1. Results of the rapid antigen and polymerase chain reaction (PCR) tests.

		PCR		
		+	−	Total
Rapid antigen	+	65	1	66
	−	38	552[a]	590
	Total	103	553	656

[a] The values of the number of participants with both negative rapid antigen and PCR tests shown in the table may be smaller than the actual values.

Among the 103 cases that were positive for the PCR test, 74 cases (71.8%) were symptomatic (Table 2). There were no significant associations between the sensitivity and the duration from the onset of the symptoms to testing (Cramer's V = 0.146, $P = 0.837$). Similarly, the sensitivity was not associated significantly with the vaccination status, kit manufacturer, sample type of PCR, or test type (in the order: Cramer's V = 0.220, $P = 0.073$; Cramer's V = 0.204; $P = 0.118$; Cramer's V = 0.217, $P = 0.108$; $\varphi = 0.012$, $P = 0.904$; Table 3). Among those whose PCR sample type was saliva (n = 80), the sensitivity was 0.58 (95% CI: 0.47–0.68).

Table 2. Associations between the sensitivity of the rapid antigen tests compared with the polymerase chain reaction (PCR) tests and the duration from the onset of the symptoms to testing, vaccination status, kit manufacturer, sample type of PCR, or test type.

Items		Rapid antigen: + PCR: +	Rapid antigen: − PCR: +	Sensitivity	φ or Cramer's V	*P*
Duration from the onset of the symptoms to testing	−2 days[a]	3	1	0.75	0.146	0.837[b]
	−1 day[a]	5	3	0.63		
	0 day	20	16	0.56		
	1 day	12	5	0.71		
	2 days	5	4	0.56		
	Asymptomatic	20	9	0.69		
Vaccination	Yes	43	27	0.61	0.220	0.073[b]
	No	9	9	0.50		
	Unknown	13	2	0.87		
Kit manufacturer	Abbott	33	12	0.73	0.204	0.118[c]
	Roche	8	9	0.47		
	Either	24	17	0.59		
Sample type of PCR	Saliva	46	34	0.58	0.217	0.108[b]
	Nasal swab	9	2	0.82		
	Either or other	10	2	0.83		
Test type	Regular	23	13	0.64	0.012	0.904[c]
	Voluntary	42	25	0.63		

[a] "−2 days" and "−1 day" represent cases that were asymptomatic at the time of tests but subsequently developed symptoms. [b] Fisher's exact test. [c] Chi-square test.

Table 3. Associations between the sensitivity of the rapid antigen tests compared with the polymerase chain reaction (PCR) tests and the duration from the onset of the symptoms to testing: a stratified analysis.

	Rapid antigen: + PCR: +	Rapid antigen: − PCR: +	Sensitivity	Cramer's V	*P*
Vaccine: yes (n=70)					
−2 days or −1 day[a]	7	3	0.70	0.084	0.955[b]
0 day	15	11	0.58		
1 day or 2 days	7	4	0.64		
Asymptomatic	14	9	0.61		
Kit manufacturer: Abbott (n=45)					
−2 days or −1 day[a]	4	3	0.57	0.181	0.688[b]
0 day	13	3	0.81		
1 day or 2 days	3	1	0.75		
Asymptomatic	13	5	0.72		
Sample type of PCR: saliva (n=80)					
−2 days or −1 day[a]	6	4	0.60	0.087	0.895[c]
0 day	16	14	0.53		
1 day or 2 days	10	8	0.56		
Asymptomatic	14	8	0.64		

[a] "−2 days or −1 day" represents cases that were asymptomatic at the time of tests but subsequently developed symptoms. [b] Fisher's exact test. [c] Chi-square test.

A stratified analysis of 70 vaccinated individuals showed no significant association between the sensitivity and the duration from the onset of the symptoms to testing (Cramer's V = 0.084, $P = 0.955$). Similarly, the stratified analysis of 45 individuals whose used Abbott and of 80 individuals whose PCR sample type was saliva showed no significant associations between the two (in the order: Cramer's V = 0.181, $P = 0.688$; Cramer's V = 0.087, $P = 0.895$).

DISCUSSION

In this study, using 656 cases, we compared the rapid antigen and PCR tests for COVID-19, that were

conducted on the same day among players and staff members of the Japan Professional Football League and clubs from January to March 2022, when the Omicron variant emerged, in order to determine the sensitivity and specificity of the rapid antigen test against the PCR test. We also investigated on the relationship between the sensitivity and the duration from the onset of the symptoms to testing, vaccination status, rapid antigen test kit manufacturer, sample type of PCR, or test type.

The sensitivity was 0.63 (95% CI: 0.54–0.72) and specificity was 0.998 (95% CI: 0.995–1.000). The specificity was possibly an underestimate because there may have been fewer reports on the number of cases that were negative for both tests than the actual number. The sensitivity was not associated significantly with the duration from the onset of the symptoms to testing. Consistent results were found in the stratified analysis of only those who were vaccinated, those whose kit manufacturer was Abbott, and those whose PCR sample type was saliva. Overall, the effect sizes were small (Cramer's $V < 0.2$). Furthermore, the sensitivity was associated insignificantly with vaccination status, kit manufacturer, sample type of PCR, or test type (Cramer's V or $\varphi \leq 0.22$).

The results obtained in this study indicated that the sensitivity of the rapid antigen test compared to the results of the PCR test was independent of the duration from infection to testing or the presence or absence of symptom onset. This result was contrast to that of the previous report (preprint) [6]: sensitivity of the rapid antigen test (Abbott or Quidel) compared with that of the PCR test (sample type: saliva) was 0.25 within two days from the first positive PCR test to the target testing and 0.9 since three days. The sensitivity in this study was higher than the sensitivity of the previous study

(i.e., 0.25 within two days from the first positive PCR test to the target testing). One possible explanation is that the players and staff members who were the participants of this study received lectures from their physicians on how to collect samples and that the tests were performed routinely, so that the samples were collected appropriately. The sensitivity of the rapid antigen tests may decrease when the tests are not performed according to the manufacturers' instructions for use [14]. Proper sample collection can lead to a high sensitivity.

The results of this study, which showed that the sensitivity of the rapid antigen test compared with the PCR test was 0.63 (95% CI: 0.54–0.72), may be used in combination with a model analysis to provide the fundamental knowledge required to establish a highly effective and efficient testing system. For example, a model analysis has estimated that the use of frequent rapid antigen testing is more effective than infrequent PCR testing in reducing the infection risk among populations such as professional sport players and staff members [15]. Under the assumption of an incubation period of five days and an R_0 of 4, the infection risk (defined as "number of infected individuals remaining at the end of the two-week isolation") among population, in which a daily rapid antigen test with a sensitivity compared with a PCR test of 0.6 that was conducted for two weeks, was estimated to be as effective as when PCR testing was performed every three days [15]. Similarly, the sensitivity of 0.5 and 0.7 was equivalent to a PCR test being performed once every four days and every two days, respectively. Since the cost of the rapid antigen test is approximately 1/10 that of the PCR test, the rapid antigen test can be performed more frequently than the PCR test under the same financial resources, and is therefore expected to be highly effective in controlling infection. However, since

the Omicron variant is more infectious than previous variants [16] and has a shorter incubation period [17], future testing strategies are expected to be combined with further model evaluations to match the characteristics of the Omicron variant.

This study had some limitations. First, the manufacturer of the test kits and the samples used in the PCR tests were based on the data provided by the clubs, and it was not possible to identify the manufacturer or sample types of some participants. In this study, however, we found that there were no significant differences in the sensitivity irrespective of the manufacturer or sample types including the groups "either" or "either or other." We also confirmed that there was no association between the sensitivity and the duration from the onset of the symptoms to testing by performing a stratified analysis of only those for whom the manufacturer was Abbott or the PCR sample type was saliva. Second, this study did not provide clinical diagnostic information on COVID-19. Therefore, it was not possible to assess the sensitivity of the rapid antigen test against the clinical diagnosis. In this regard, however, PCR test was world-widely used as the gold standard to diagnose COVID-19. We therefore assessed the sensitivity of the rapid antigen test compared with the PCR test. Third, we could not obtain information on the participants' age, gender, presence or absence of underlying diseases, and history of COVID-19 infection. The Ct values for the PCR tests were also only available from some of the participants. Therefore, it was not possible to evaluate the association between the sensitivity of these items. Fourth, SARS-CoV-2 viruses were not sequenced to confirm them as the Omicron variant. However, since the Omicron variant was predominant in the period under study (98.92% [11]) as described above, the possibility of other variants was very low. Fifth, the participants

of this study were professional sport players and staff members and are therefore considered, in general, to be a healthy population. Cautions are therefore required in applying the findings of this study in populations with different characteristics, such as children, elderly, and those with underlying diseases.

Despite such limitations, this study analyzed the sensitivity and specificity of the rapid antigen test against the PCR test during the Omicron variant outbreak, and found that the sensitivity was independent of the duration from the onset of the symptoms to testing.

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Contributors

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Writing –original draft: M.M.

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Competing interests

H.S. and T. I. received salaries by from the Japan Professional Football League. W.N. and T.Y. have received financial support from the Japan Professional Football League, the Yomiuri Giants, Tokyo Yakult Swallows, the Japan Professional Basketball League, and the Kao Corporation in the context of measures at mass-gathering events. M.M., M.K., W.N, T.Y., and S.I. have attended the New Coronavirus Countermeasures Liaison Council jointly established by the Nippon Professional Baseball Organization and the Japan Professional Football League as experts without any reward. W.N. and T.Y. were/are advisors to the Japan National Stadium and Japan Professional Football League. The data used in this study were provided from the Japan Professional Football League. Otherwise, these institutions had no role in study design. The findings and conclusions of this article are solely the responsibility of the authors and do not represent the official views of any institution.

Data availability statement

We have included all the data produced in the present work in the manuscript. Note that the raw data used in the study were provided by Japan Professional Football League, as described in this paper. We are unable to attach all the raw data for each participant in this paper due to the ethical restrictions.

Notes

This article has already been registered for Preprints on medRxiv.

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(https://www.medrxiv.org/content/10.1101/2022.06.13.22276325v1).

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-9
Bias	9	Describe any efforts to address potential sources of bias	6-9
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	na
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9-11
		(b) Give reasons for non-participation at each stage	na
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11
		(b) Indicate number of participants with missing data for each variable of interest	na
Outcome data	15*	Report numbers of outcome events or summary measures	9-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11

		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	12-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Sensitivity of rapid antigen tests for COVID-19 during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs: A retrospective observational study

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Sensitivity of rapid antigen tests for COVID-19 during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs: A retrospective observational study

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Abstract

Objectives

Rapid antigen tests have been used to prevent the spread of the coronavirus disease 2019 (COVID-19); however, there have been concerns about their decreased sensitivity to the Omicron variant. In this study, we assessed the sensitivity and specificity of the rapid antigen test compared with the polymerase chain reaction (PCR) test among the players and staff members of the Japan Professional Football League and clubs. Furthermore, we evaluated the relationship between the sensitivity and the duration from the onset of symptoms to testing or vaccine status.

Design

This was a retrospective observational study.

Methods

We used 656 results from both the rapid antigen and PCR tests for COVID-19 using samples collected on the same day from January 12 to March 2, 2022, during the Omicron variant outbreak in Japan.

Results

The sensitivity of the rapid antigen test compared with the PCR test was 0.63 (95% confidence interval: [CI] 0.53–0.73) and the specificity was 0.998 (95%CI: 0.995–1.000). There were no significant associations between the sensitivity and the duration from the onset of symptoms to testing (including asymptomatic cases in the category) or vaccination status ($P > 0.05$) with small effect sizes (Cramer's V or φ: ≤ 0.22).

Conclusions

Even during the Omicron outbreak, the sensitivity of the rapid antigen tests did not depend on the duration from the onset of symptoms to testing.

Strengths and limitations of this study

- We obtained the results from both rapid antigen and PCR tests for COVID-19 using the samples collected on the same day during the Omicron variant outbreak among the players and staff of the Japan Professional Football League and clubs.
- We assessed the sensitivity and specificity of the rapid antigen test against the PCR test.
- We analyzed the association between the sensitivity and the duration from the onset of symptoms to testing.
- Since the participants were professional sport players and staff members, cautions are required in applying the findings of this study in general or other populations.

INTRODUCTION

To prevent the spread of the coronavirus disease 2019 (COVID-19), active testing has been used to identify and isolate infected individuals, especially in populations at high risk of infections [1]. Among the various testing methods including the reverse transcription-polymerase chain reaction (PCR) test, antigen quantitative test, and rapid antigen test, the rapid antigen test is the least sensitive, but it has the advantage of being inexpensive and providing prompt test results [2]. In particular, highly-frequent routine testing using rapid antigen test kits is more promising in reducing the spread of infection than highly-sensitive, but low-frequent testing [3]. It has been noted; however, that the sensitivity of the rapid antigen tests may be lower with Omicron variants than previous variants [4 5]. In addition, the sensitivity of the rapid antigen tests may be particularly low during the first few days after infection (preprint)[6]. Since the testing and identification of infected individuals is more effective in controlling the spread of infection during the short period between infection and testing, there is concern that the lower sensitivity of the rapid antigen tests during the short period after infection may reduce the effectiveness of the testing system in the population. However, contrary to this, a previous study reported no large differences in the analytical sensitivity of the rapid antigen test in a comparison between representative Delta and Omicron isolates, using ten test kits [7]. In another case study with human participants, there was also no difference in the sensitivity of the rapid antigen test between the Delta and Omicron variants (preprint) [8]. Since both rapid antigen tests and other tests (e.g. PCR tests) must be performed using the samples collected on the same day from the same individuals to evaluate the sensitivity of the rapid antigen tests, studies based on human participants have been

limited [9] and these findings were not sufficient.

The Japan Professional Football League, a professional league of the most popular sport in Japan, collected the results of rapid antigen and PCR tests for COVID-19 among players and staff members in order to maintain and promote its activities [10]. If the rapid antigen test was positive, the person was required to remain at home until the results of the PCR test or the physician's diagnosis were obtained. If the PCR test was positive, the patient had to visit a medical institution. Since January 2022, rapid antigen testing was conducted twice a week on a regular basis, and moreover, additional PCR testing was often conducted on players and staff members in the clubs where infected individuals were identified. Consequently, from January 12 to March 2, 2022, during the period when the Omicron variants emerged in Japan, the number of cases in which both rapid antigen and PCR tests were performed on the same day exceeded 650, which made it possible to evaluate the sensitivity of the rapid antigen test compared with the PCR test.

In this study, we compared the results between the rapid antigen and PCR tests for COVID-19 among the players and staff of the Japan Professional Football League and clubs to determine the sensitivity and specificity of the rapid antigen test against the PCR test. We then assessed the relationships between the sensitivity and the duration from the onset of symptoms to testing, or vaccine status.

METHODS

Participants

This study was a retrospective observational study. We obtained the test results from January 12, to

March 2, 2022. This was the period of the Omicron variant outbreaks in Japan (98.92% on February 7, 2022) [11]. The data included a total of 656 cases in which both rapid antigen and PCR tests were performed using the samples collected on the same date from players and staff members of the Japan Professional Football League and clubs. In total, Japan Professional Football League and clubs had 1,759 players and 1,864 staff members (as of February, 2022). Each club has its own testing manager and physician. Among 58 clubs from J1 (the highest grade) to J3 (the lowest grade) in Japan Professional Football League, 23 clubs were included in this study. Since personal information on the participants was not available, the breakdown of the number of players and staff members in 656 cases was unknown. In the process of collecting the test results from players and staff members, some of the cases in which both tests were negative may not have been available: i.e., the number of cases reported in this study in which both tests were negative may have been smaller than the actual number.

Survey items

The information used in this study included the positivity or negativity of each test, the presence or absence of symptoms, duration between the onset of symptoms and testing, vaccination status (i.e., whether the participants were vaccinated: at least once, none, or unknown), the manufacturer of the rapid antigen test kit, the sample types of the PCR test (i.e., “saliva,” “nasal swab,” or “either or other”), and the type of test (“regular test,” defined by the use of a routine rapid antigen test twice a week by the Japan Professional Football League or a “voluntary test” other than a routine test). The onset of symptoms was based on the tally by the Japan Professional Football League, which

comprised the individuals' self-reported information that their health condition was different from usual (e.g., fever, sore throat). The date of the onset of symptoms represented the date when the symptom developed. Asymptomatic cases represented those who did not exhibit symptoms up to the time of testing and after.

The rapid antigen test was performed using nasal swab samples, and the kits were the Abbott Panbio™ COVID-19 Antigen Rapid Test or the Roche SARS-CoV-2 Rapid Antigen Test. The sample types of the PCR test were saliva or a nasal swab. Both samples were generally self-collected by the participants except some rare cases of collection by the testing managers or physicians. The samples for the rapid antigen and PCR tests were collected and analyzed separately. No samples were pooled. The players and staff members of the Japan Professional Football League and the clubs received lectures from their physicians on how to collect samples. Each club sent their samples to a medical or measuring laboratory for PCR testing. A Ct (threshold cycle) value of < 40 was considered as positive. PCR test results were notified from 2 hours to the next day after sample collection. Other details of the analytical information of the PCR tests were not available. Since information on the manufacturer of the rapid antigen test kits and on the sample types of PCR was not available on an individual basis, we instead matched the individuals and their club using the information that was obtained from a survey of how each club conducted testing during the period. The clubs determined whether the manufacturer of the rapid antigen test kit was Abbott, Roche, or either, and whether the sample types of PCR were saliva, nasal swab, either, or other. The results (positivity or negativity) of the rapid antigen test among each of the 103 PCR-positive cases according to the duration from the

onset of symptoms to testing (including asymptomatic cases in the category) were reported on the website of the Japan Professional Football League [12].

Patient and public involvement

Patients and the public were not involved in the design, or conduct of the study. The information about this study was disclosed on the websites of the Institute of Medical Science of the University of Tokyo and the Japan Professional Football League.

Statistical analysis

In this study, the sensitivity and specificity of the rapid antigen test against the PCR test were first calculated by comparing the results (positivity or negativity) between both tests. We performed a Bootstrap method (10,000 samples) to estimate the 95% confidence interval (CI) of sensitivity and specificity. We also used the Bootstrap method (10,000 samples) to estimate the 95% CI of sensitivity among only those whose PCR sample type was saliva (n = 80). Next, among the cases with positive PCR results, the chi-squared test or Fisher's exact test was performed to investigate the associations between the results of the rapid antigen test (positivity or negativity) and the duration from the onset of symptoms to testing (including asymptomatic cases in the category), vaccination status or test type. As an additional stratified analysis, only vaccinated individuals, those whose rapid antigen test kit manufacturer was Abbott, and those whose PCR sample type was saliva were used to examine the relationships between the rapid antigen test result (positivity or negativity) and the duration from the

onset of symptoms to testing (in categories asymptomatic included) using the chi-squared test or Fisher's exact test. In this stratified analysis, −2 and −1 days were grouped together as one category for the duration from the onset of symptoms to testing. Similarly, 1 and 2 days were combined into one category.

IBM SPSS version 28 and R 4.2.0 [13] were used for the statistical analysis.

RESULTS

Of the 656 cases, 65 were positive for both the rapid antigen and PCR tests, 38 negative for the antigen tests and positive for the PCR test, one was positive for the rapid antigen test and negative for the PCR test, and 552 were negative for both (Table 1). The sensitivity of the rapid antigen test compared with the PCR test was 0.63 (95%CI: 0.53–0.73) and the specificity was 0.998 (95% CI: 0.995–1.000).

Table 1. Results of the rapid antigen and polymerase chain reaction (PCR) tests. The sensitivity and specificity was 0.63 (95% confidence interval: 0.53–0.73) and 0.998 (0.995–1.000), respectively.

		PCR		
		+	−	Total
Rapid antigen	+	65 (63%)	1 (0.2%)	66
	−	38 (37%)	552 (99.8%)[a]	590
	Total	103 (100%)	553 (100%)	656

[a] The values of the number of participants with both negative rapid antigen and PCR tests shown in the table may be smaller than the actual values. See the details in "**Participants**" in **METHODS**.

Among the 103 cases that were positive for the PCR test, 74 cases (71.8%) were symptomatic (Table

2). There were no significant associations between the sensitivity and the duration from the onset of symptoms to testing (Cramer's V = 0.146, $P = 0.837$). Similarly, the sensitivity was not associated significantly with the vaccination status or test type (in the order: Cramer's V = 0.220, $P = 0.073$; φ = 0.012, $P = 0.904$). Among those whose PCR sample type was saliva (n = 80), the sensitivity was 0.58 (95% CI: 0.46–0.69).

Table 2. Associations between the sensitivity of the rapid antigen test compared with the polymerase chain reaction (PCR) test and the duration from the onset of symptoms to testing, vaccination status, kit manufacturer, sample type of PCR, or test type.

Items		Rapid antigen: + PCR: +	Rapid antigen: − PCR: +	Sensitivity	φ or Cramer's V	*P*
Duration from the onset of symptoms to testing	−2 days[a]	3	1	0.75	0.146	0.837[b]
	−1 day[a]	5	3	0.63		
	0 day	20	16	0.56		
	1 day	12	5	0.71		
	2 days	5	4	0.56		
	Asymptomatic	20	9	0.69		
Vaccination	Yes	43	27	0.61	0.220	0.073[b]
	No	9	9	0.50		
	Unknown	13	2	0.87		
Test type	Regular	23	13	0.64	0.012	0.904[c]
	Voluntary	42	25	0.63		

[a] "−2 days" and "−1 day" represent cases that were asymptomatic at the time of tests but subsequently developed symptoms. [b] Fisher's exact test. [c] Chi-squared test.

Table 3. Associations between the sensitivity of the rapid antigen test compared with the polymerase chain reaction (PCR) test and the duration from the onset of symptoms to testing: a stratified analysis.

	Rapid antigen: + PCR: +	Rapid antigen: − PCR: +	Sensitivity	Cramer's V	*P*
Vaccine: yes (n=70)					
−2 days or −1 day[a]	7	3	0.70	0.084	0.955[b]
0 day	15	11	0.58		
1 day or 2 days	7	4	0.64		
Asymptomatic	14	9	0.61		
Kit manufacturer: Abbott (n=45)					
−2 days or −1 day[a]	4	3	0.57	0.181	0.688[b]
0 day	13	3	0.81		
1 day or 2 days	3	1	0.75		
Asymptomatic	13	5	0.72		
Sample type of PCR: saliva (n=80)					
−2 days or −1 day[a]	6	4	0.60	0.087	0.895[c]
0 day	16	14	0.53		
1 day or 2 days	10	8	0.56		
Asymptomatic	14	8	0.64		

[a] "−2 days or −1 day" represents cases that were asymptomatic at the time of tests but subsequently developed symptoms. [b] Fisher's exact test. [c] Chi-squared test.

A stratified analysis of 70 vaccinated individuals showed no significant association between the sensitivity and the duration from the onset of symptoms to testing (Cramer's V = 0.084, $P = 0.955$; Table 3). Similarly, the stratified analysis of 45 individuals whose used Abbott and of 80 individuals whose PCR sample type was saliva showed no significant associations between the two (in the order: Cramer's V = 0.181, $P = 0.688$; Cramer's V = 0.087, $P = 0.895$).

DISCUSSION

Using 656 cases, we compared the rapid antigen and PCR test results for COVID-19, that were

conducted on the same day among players and staff members of the Japan Professional Football League and clubs from January to March 2022, when the Omicron variant emerged, in order to determine the sensitivity and specificity of the rapid antigen test against the PCR test. We also investigated the relationship between the sensitivity and the duration from the onset of symptoms to testing, vaccination status or test type.

The sensitivity was 0.63 (95% CI: 0.53–0.73) and specificity was 0.998 (95% CI: 0.995–1.000). The specificity was possibly an underestimate because there may have been fewer reports on the number of cases that were negative for both tests than the actual number. The sensitivity was not associated significantly with the duration from the onset of symptoms to testing. Consistent results were found in the stratified analysis of only those who were vaccinated, those whose kit manufacturer was Abbott, and those whose PCR sample type was saliva. Overall, the effect sizes were small (Cramer's $V < 0.2$). Furthermore, the sensitivity was not associated with vaccination status or test type (Cramer's V or $\varphi \leq 0.22$).

The results indicated that the sensitivity of the rapid antigen test compared to the results of the PCR test was independent of the duration from infection to testing or the presence or absence of symptom onset. This result was in contrast to that of a previous report (preprint) [6]: sensitivity of the rapid antigen test (Abbott or Quidel) compared with that of the PCR test (sample type: saliva) was 0.25 within 2 days from the first positive PCR test to the target testing and 0.9 since 3 days. The sensitivity in our study was higher than the sensitivity of the previous study (i.e., 0.25 within 2 days from the first positive PCR test to the target testing). One possible explanation is that the players and staff

members who were the participants of our study received lectures from their physicians on how to collect samples and that the tests were performed routinely, so that the samples were collected appropriately. The sensitivity of the rapid antigen tests may decrease when the tests are not performed according to the manufacturers' instructions for use [14]. Proper sample collection can lead to a high sensitivity.

The results of our study, which showed that the sensitivity of the rapid antigen test compared with the PCR test was 0.63 (95% CI: 0.53–0.73), may be used in combination with a model analysis to provide the fundamental knowledge required to establish a highly effective and efficient testing system. For example, a model analysis has estimated that the use of frequent rapid antigen testing is more effective than infrequent PCR testing in reducing the infection risk among populations such as professional sports players and staff members [15]. Under the assumption of an incubation period of 5 days and an R_0 of 4, the infection risk (defined as "number of infected individuals remaining at the end of the 2-week isolation") among populations, in which a daily rapid antigen test with a sensitivity compared with a PCR test of 0.6 that was conducted for 2 weeks, was estimated to be as effective as when PCR testing was performed every 3 days [15]. Similarly, the sensitivity of 0.5 and 0.7 was equivalent to a PCR test being performed once every 4 days and every 2 days, respectively. Since the cost of the rapid antigen test is approximately one tenth that of the PCR test, the rapid antigen test can be performed more frequently than the PCR test assuming the same financial resources, and is therefore expected to be highly effective in controlling infection. However, since the Omicron variant is more infectious than previous variants [16] and has a shorter incubation period [17], future testing

strategies are expected to be combined with further model evaluations to match the characteristics of the Omicron variant.

Our study had some limitations. First, the manufacturer of the test kits and the samples used in the PCR tests were based on the data provided by the clubs, and it was not possible to identify the manufacturer or sample types used by some participants. Therefore, we did not analyze the association between the sensitivity and the manufacturer or sample types. However, we confirmed that there was no association between the sensitivity and the duration from the onset of symptoms to testing by performing a stratified analysis of only those for whom the manufacturer was Abbott or the PCR sample type was saliva. Second, this study did not provide clinical diagnostic information on COVID-19. Therefore, it was not possible to assess the sensitivity of the rapid antigen test against the clinical diagnosis. In this regard, however, the PCR test is used world-wide as the gold standard to diagnose COVID-19. We therefore assessed the sensitivity of the rapid antigen test compared with the PCR test. Third, we could not obtain information on the participants' age, gender, presence or absence of underlying diseases, and history of COVID-19 infection. The Ct values for the PCR tests were also only available from some of the participants. Therefore, it was not possible to evaluate the association between the sensitivity of these items. Fourth, SARS-CoV-2 viruses were not sequenced to confirm them as the Omicron variant. However, since the Omicron variant was predominant in the period under study (98.92% [11]) as described above, the possibility of other variants was very low. Fifth, the participants of this study were professional sports players and staff members who are therefore considered, in general, to be a healthy population. Cautions are therefore required in

applying the findings of our study to populations with different characteristics, such as children, the elderly, and those with underlying diseases.

Despite such limitations, we analyzed the sensitivity and specificity of the rapid antigen test against the PCR test during the Omicron variant outbreak, and found that the sensitivity was independent of the duration from the onset of symptoms to testing.

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Contributors

M.M., H.S., T.I., M.K., W.N., T.Y., and S.I. contributed to the conception of the study. H.S. and T.I. contributed to data curation. M.M. contributed to formal analysis, methodology, and visualization. S.I. contributed to supervision and project administration. M.M. drafted the manuscript. H.S., T.I., M.K., W.N., T.Y., and S.I. reviewed and edited the manuscript.

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Competing interests

H.S. and T. I. received salaries from the Japan Professional Football League. W.N. and T.Y. have

received financial support from the Japan Professional Football League, the Yomiuri Giants, Tokyo Yakult Swallows, the Japan Professional Basketball League, and the Kao Corporation in the context of measures at mass-gathering events. M.M., M.K., W.N, T.Y., and S.I. have attended the New Coronavirus Countermeasures Liaison Council jointly established by the Nippon Professional Baseball Organization and the Japan Professional Football League as experts without any reward. W.N. and T.Y. were/are advisors to the Japan National Stadium and Japan Professional Football League. The data used in this study were provided from the Japan Professional Football League. Otherwise, these institutions had no role in study design. The findings and conclusions of this article are solely the responsibility of the authors and do not represent the official views of any institution.

Data availability statement

We have included all the data produced in the present work in the manuscript. Note that the raw data used in the study were provided by Japan Professional Football League, as described in this paper. We are unable to attach all the raw data for each participant in this paper due to the ethical restrictions.

Notes

This article has already been registered for Preprints on medRxiv.

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Ethics approval

This study was conducted with the approval of the Ethics Review Committee of the Institute of Medical Science, University of Tokyo (approval number 2022-1-0421). Testing was not conducted originally for research purposes and the Japan Professional Football League does not have personal information relating to all results. Therefore, information about this study was disclosed on the websites of the Institute of Medical Science of the University of Tokyo and the Japan Professional Football League to provide participants with the opportunity to opt out of the study. The person in charge of each club also provided information about the study to potential participants (players and staff members).

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1,2 [in the cleaned manuscript]
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-9
Bias	9	Describe any efforts to address potential sources of bias	6-9
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	na
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8-9
		(*e*) Describe any sensitivity analyses	8-9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9-11
		(b) Give reasons for non-participation at each stage	na
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11

		(b) Indicate number of participants with missing data for each variable of interest	na
Outcome data	15*	Report numbers of outcome events or summary measures	9-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11
		(*b*) Report category boundaries when continuous variables were categorized	9-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14-15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Sensitivity of rapid antigen tests for COVID-19 during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs: A retrospective observational study

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Sensitivity of rapid antigen tests for COVID-19 during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs: A retrospective observational study

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Abstract

Objectives

Rapid antigen tests have been used to prevent the spread of the coronavirus disease 2019 (COVID-19); however, there have been concerns about their decreased sensitivity to the Omicron variant. In this study, we assessed the sensitivity and specificity of the rapid antigen test compared with the polymerase chain reaction (PCR) test among the players and staff members of the Japan Professional Football League and clubs. Furthermore, we evaluated the relationship between the sensitivity and the duration from the onset of symptoms to testing or vaccine status.

Design

This was a retrospective observational study.

Methods

We used 656 results from both the rapid antigen and PCR tests for COVID-19 using samples collected on the same day from January 12 to March 2, 2022, during the Omicron variant outbreak in Japan.

Results

The sensitivity of the rapid antigen test compared with the PCR test was 0.63 (95% confidence interval: [CI] 0.53–0.73) and the specificity was 0.998 (95% CI: 0.995–1.000). There were no significant associations between the sensitivity and the duration from the onset of symptoms to testing (including asymptomatic cases in the category) or vaccination status ($P > 0.05$) with small effect sizes (Cramer's V or φ: ≤ 0.22).

Conclusions

Even during the Omicron outbreak, the sensitivity of the rapid antigen tests did not depend on the duration from the onset of symptoms to testing.

Strengths and limitations of this study

- Rapid antigen testing was conducted twice weekly on a regular basis during the Omicron variant outbreak among the players and staff of the Japan Professional Football League and clubs, and moreover, additional antigen and PCR testing was conducted in the clubs where infected individuals were identified.
- We obtained the results from both rapid antigen and PCR tests for COVID-19 using samples collected on the same day.
- We had a sufficient number of participants to examine the association between the sensitivity of the rapid antigen test and the duration from the onset of symptoms to testing.
- Not all rapid antigen tests could be paired with PCR tests with the same date.
- No information on individual characteristics potentially related to sensitivity and specificity was available.

INTRODUCTION

To prevent the spread of the coronavirus disease 2019 (COVID-19), active testing has been used to identify and isolate infected individuals, especially in populations at high risk of infection [1]. Among the various testing methods including the reverse transcription-polymerase chain reaction (PCR) test, antigen quantitative test, and rapid antigen test, the rapid antigen test is the least sensitive, but it has the advantage of being inexpensive and providing prompt test results [2]. In particular, high-frequency routine testing using rapid antigen test kits is more promising in reducing the spread of infection than highly-sensitive, but low-frequency testing, because it can identify infected individuals from the time of infection until the onset of symptoms (i.e., presymtomatic cases), when a high viral load is present [3]. It has been noted; however, that the sensitivity of the rapid antigen tests may be lower for Omicron than for previous variants [4 5]. In addition, the sensitivity of the rapid antigen tests may be particularly low during the first few days after infection (preprint) [6]. This means that rapid antigen testing may be less effective in identifying infected individuals with high viral load prior to the onset of symptoms during the Omicron variant outbreak. Thus, there is concern that the lower sensitivity of the rapid antigen tests during the short period after infection may reduce the effectiveness of the testing system in the population. However, it is not clear whether the sensitivity of rapid antigen tests is lower for Omicron than for previous variants. A previous study reported no large differences in the analytical sensitivity of the rapid antigen test in a comparison between representative Delta and Omicron isolates, using ten test kits [7]. In another case study with human participants, there was also no difference in the rapid antigen test sensitivity between the Delta and Omicron variants [8]. Since both

rapid antigen and other tests (e.g. PCR tests) must be performed using samples collected on the same day from the same individuals to evaluate the sensitivity of the rapid antigen tests, studies based on human participants have been limited [9] and these findings were not sufficient.

The Japan Professional Football League, a professional league of the most popular sport in Japan, collected the results of rapid antigen and PCR tests for COVID-19 among players and staff members in order to maintain and promote its activities [10]. If the rapid antigen test was positive, the person was required to remain at home until the results of the PCR test or the physician's diagnosis were obtained. If the PCR test was positive, the patient had to visit a medical institution. Since January 2022, rapid antigen testing was conducted twice a week on a regular basis. Moreover, additional antigen and PCR testing was often conducted on players and staff members in the clubs where infected individuals were identified. Consequently, from January 12 to March 2, 2022, during the period when the Omicron variants emerged in Japan, the number of cases in which both rapid antigen and PCR tests were performed on the same day exceeded 650, which made it possible to evaluate the sensitivity of the rapid antigen test compared with the PCR test.

In this study, we compared the results between the rapid antigen and PCR tests for COVID-19 among the players and staff of the Japan Professional Football League and clubs to determine the sensitivity and specificity of the rapid antigen test against the PCR test. We then assessed the relationships between the sensitivity and the duration from the onset of symptoms to testing, or vaccine status.

METHODS

Participants

This study was a retrospective observational study. We obtained test results from January 12, to March 2, 2022. This was the period of the Omicron variant outbreaks in Japan (98.92% on February 7, 2022) [11]. In total, the Japan Professional Football League and clubs had 1,759 players and 1,864 staff members (as of February 2022). Each club has its own testing manager and physician. The Japan Professional Football League conducted a routine rapid antigen test (hereinafter, "regular test") twice weekly among players and staff members (a total of 35,393 tests during the study period). Each club also conducted additional rapid antigen testing (hereinafter, "voluntary test") and PCR testing, but the number of such tests was not available. We obtained the data including a total of 656 cases in which both rapid antigen and PCR tests were performed using samples collected on the same date from players and staff members of the Japan Professional Football League and clubs (Figure 1). If the rapid antigen and PCR tests were performed on different dates, they were not included in this study. Of the 656 cases, 277 were regular tests and 379 were voluntary tests. Among 58 clubs from J1 (the highest grade) to J3 (the lowest grade) in the Japan Professional Football League, 23 clubs (707 players and 754 staff members, as of February 2022) were included in this study as a result. Since personal information on the participants was not available, the breakdown of the number of players and staff members in 656 cases was unknown. In the process of collecting the test results from players and staff members, some of the cases in which both tests were negative may not have been available: i.e., the number of cases reported in this study in which both tests were negative may be smaller than the actual number.

Table 1 shows the date and number of cases per club covered in this study. The same person was never subjected to rapid antigen or PCR tests more than once on the same day: the number of cases assessed in a given club on a given day represents the number of unique participants (no duplicates). Therefore, the maximum number of cases assessed on a given day in each club represents the minimum possible number of unique participants in the club. Furthermore, the same person did not belong to different clubs. Hence, the sum of the minimum possible number of unique participants in clubs (n = 309) represents the minimum possible number of unique participants in this study.

Table 1. The date and number of tests per club, and minimum possible number of unique participants during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs. n: number of cases in which both rapid antigen and PCR tests were performed on the same date.

Club number	Date (n)	n (total)	Minimum possible number of unique participants
1	Jan. 12 (2); Jan. 19 (1); Jan. 21 (1)	4	2
2	Jan. 12 (1)	1	1
3	Jan. 20 (1); Jan. 27 (1); Jan. 31 (1)	3	1
4	Jan. 24 (47); Jan. 28 (46); Jan. 30 (2); Feb. 4 (40); Feb. 22 (1); Feb. 28 (2)	138	47
5	Jan. 19 (14); Jan 20 (2); Jan. 22 (12); Jan. 27 (1); Jan. 28 (1)	30	14
6	Jan. 30 (2); Jan. 31 (3); Feb. 2 (1)	6	3
7	Jan. 30 (3); Feb. 3 (1)	4	3
8	Feb. 4 (2); Feb. 7 (1)	3	2
9	Feb. 8 (49); Feb. 10 (1); Feb. 12 (4)	54	49
10	Feb. 12 (1); Feb. 15 (1); Feb. 17 (1); Feb. 18 (1)	4	1
11	Feb. 7 (1); Feb. 16 (2); Feb. 22 (37)	40	37
12	Feb. 14 (1); Feb. 16 (3); Feb. 20 (13)	17	13
13	Feb. 20 (1); Feb. 22 (1); Feb. 24 (1); Feb. 28 (3)	6	3
14	Feb. 21 (4); Feb. 24 (2); Feb. 25 (1); Feb. 26 (1); Mar. 1 (1); Mar. 2 (4)	13	4
15	Feb. 26 (5)	5	5
16	Mar. 2 (1)	1	1
17	Feb. 15 (4); Feb. 16 (1); Feb. 21 (3); Feb. 22 (3)	11	4
18	Feb. 21 (3)	3	3
19	Jan. 29 (1)	1	1
20	Jan. 23 (58); Jan. 24 (58); Jan. 25 (6); Jan. 26 (3); Jan. 27 (53); Jan. 28 (4); Jan. 30 (4); Jan. 31 (6); Feb. 3 (8)	200	58
21	Feb. 5 (52); Feb. 8 (50); Feb. 11 (1)	103	52
22	Jan. 12 (1); Jan. 15 (3); Jan. 17 (3)	7	3
23	Feb. 18 (2)	2	2
Total		656	309

Survey items

The information used in this study included the positivity or negativity of each test, presence or absence of symptoms, duration between the onset of symptoms and testing, vaccination status (i.e.,

whether the participants were vaccinated: at least once, none, or unknown), manufacturer of the rapid antigen test kit, sample types used in the PCR test (i.e., "saliva," "nasal swab," or "either or other"), and the type of test ("regular test," defined by the use of a routine rapid antigen test twice a week by the Japan Professional Football League or a "voluntary test" other than a routine test). The onset of symptoms was based on the tally by the Japan Professional Football League, which comprised the individuals' self-reported information that their health condition was different from usual (e.g., fever, sore throat). The date of the onset of symptoms represented the date when the symptom developed. "−2 days" and "−1 day" represents 2 days or a day before symptom onset (i.e., presymtomatic cases), respectively. Asymptomatic cases represented those who did not exhibit symptoms up to the time of testing and after.

The rapid antigen test was performed using nasal swab samples, and the kits used were the Abbott Panbio™ COVID-19 Antigen Rapid Test or the Roche SARS-CoV-2 Rapid Antigen Test. The sample types used in the PCR test were saliva or a nasal swab. Both samples were generally self-collected by the participants except for some rare cases of collection by the testing managers or physicians. The samples for the rapid antigen and PCR tests were collected and analyzed separately. No samples were pooled. The players and staff members of the Japan Professional Football League and the clubs received lectures from their physicians on how to collect samples. Each club sent their samples to a medical or measuring laboratory for PCR testing. A Ct (threshold cycle) value of <40 was considered as positive. PCR test results were notified from 2 hours to the next day following sample collection. Other details of the analytical information of the PCR tests were not available.

Since information on the manufacturer of the rapid antigen test kits and on the sample types used in PCR test was not available on an individual basis, we instead matched the individuals and their club using the information that was obtained from a survey of how each club conducted testing during the period. The clubs determined whether the manufacturer of the rapid antigen test kit was Abbott, Roche, or either (i.e., sometimes Abbott, sometimes Roche), and whether the sample types used in PCR test were saliva, nasal swab, either (i.e., sometimes saliva, sometimes nasal swab), or other. The results (positivity or negativity) of the rapid antigen test among each of the 103 PCR-positive cases according to the duration from the onset of symptoms to testing (including asymptomatic cases in the category) were reported on the website of the Japan Professional Football League [12].

Patient and public involvement

Patients and the public were not involved in the design, or conduct of the study. The information about this study was disclosed on the websites of the Institute of Medical Science of the University of Tokyo and the Japan Professional Football League.

Statistical analysis

In this study, the sensitivity and specificity of the rapid antigen test against the PCR test were first calculated by comparing the results (positivity or negativity) between both tests. We performed a Bootstrap method (10,000 samples) to estimate the 95% confidence interval (CI) for sensitivity and specificity. We also used the Bootstrap method (10,000 samples) to estimate the 95% CI for

sensitivity among only those whose PCR sample type was saliva (n = 80). Next, among the cases with positive PCR results, the chi-square or Fisher's exact test was performed to investigate the associations between the results of the rapid antigen test (positivity or negativity) and the duration from the onset of symptoms to testing (including asymptomatic cases in the category), vaccination status, or test type. As an additional stratified analysis, only vaccinated individuals, those whose rapid antigen test kit manufacturer was Abbott, and those whose PCR sample type was saliva were used to examine the relationships between the rapid antigen test result (positivity or negativity) and the duration from the onset of symptoms to testing (in categories asymptomatic included) using the chi-square or Fisher's exact test. In this stratified analysis, −2 and −1 days were grouped together as one category for the duration from the onset of symptoms to testing. Similarly, 1 and 2 days were combined into one category.

IBM SPSS version 28 and R 4.2.0 [13] were used for the statistical analysis.

RESULTS

Of the 656 cases, 65 were positive for both the rapid antigen and PCR tests, 38 were negative for the antigen tests and positive for the PCR test, one was positive for the rapid antigen test and negative for the PCR test, and 552 were negative for both (Table 2). The sensitivity of the rapid antigen test compared with the PCR test was 0.63 (95% CI: 0.53–0.73) and the specificity was 0.998 (95% CI: 0.995–1.000).

Table 2. Results of the rapid antigen and polymerase chain reaction (PCR) tests during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs.

		PCR		
		+	−	Total
Rapid antigen	+	65 (63%)	1 (0.2%)	66
	−	38 (37%)	552 (99.8%)[a]	590
	Total	103 (100%)	553 (100%)	656

[a] The values of the number of participants with both negative rapid antigen and PCR tests shown in the table may be smaller than the actual values. Some of the cases in which both tests were negative may not have been reported to the Japan Professional Football League.

Among the 103 cases that were positive for the PCR test, 74 cases (71.8%) were symptomatic (Table 3). There were no significant associations between the sensitivity and the duration from the onset of symptoms to testing (Cramer's V = 0.146, $P = 0.837$). Similarly, the sensitivity was not associated significantly with the vaccination status or test type (in the order: Cramer's V = 0.220, $P = 0.073$; φ = 0.012, $P = 0.904$). Among those whose PCR sample type was saliva (n = 80), the sensitivity was 0.58 (95% CI: 0.46–0.69).

Table 3. Associations between the sensitivity of the rapid antigen test compared with the polymerase chain reaction (PCR) test and the duration from the onset of symptoms to testing, vaccination status, kit manufacturer, sample type of PCR, or test type during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs.

Items		Rapid antigen: + PCR: +	Rapid antigen: − PCR: +	Sensitivity	φ or Cramer's V	*P*
Duration from the onset of symptoms to testing	−2 days[a]	3	1	0.75	0.146	0.837[b]
	−1 day[a]	5	3	0.63		
	0 day	20	16	0.56		
	1 day	12	5	0.71		
	2 days	5	4	0.56		
	Asymptomatic	20	9	0.69		
Vaccination	Yes	43	27	0.61	0.220	0.073[b]
	No	9	9	0.50		
	Unknown	13	2	0.87		
Test type	Regular	23	13	0.64	0.012	0.904[c]
	Voluntary	42	25	0.63		

[a] "−2 days" and "−1 day" represent cases that were asymptomatic at the time of tests but subsequently developed symptoms. [b] Fisher's exact test. [c] Chi-square test.

Table 4. Associations between the sensitivity of the rapid antigen test compared with the polymerase chain reaction (PCR) test and the duration from the onset of symptoms to testing during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs: a stratified analysis.

Participants	Duration from the onset of symptoms to testing	Rapid antigen: + PCR: +	Rapid antigen: − PCR: +	Sensitivity	Cramer's V	*P*
Vaccine: yes (n=70)	−2 days or −1 day[a]	7	3	0.70	0.084	0.955[b]
	0 day	15	11	0.58		
	1 day or 2 days	7	4	0.64		
	Asymptomatic	14	9	0.61		
Kit manufacturer: Abbott (n=45)	−2 days or −1 day[a]	4	3	0.57	0.181	0.688[b]
	0 day	13	3	0.81		
	1 day or 2 days	3	1	0.75		
	Asymptomatic	13	5	0.72		
Sample type of PCR: saliva (n=80)	−2 days or −1 day[a]	6	4	0.60	0.087	0.895[c]
	0 day	16	14	0.53		
	1 day or 2 days	10	8	0.56		
	Asymptomatic	14	8	0.64		

[a] "−2 days or −1 day" represents cases that were asymptomatic at the time of the tests but subsequently developed symptoms. [b] Fisher's exact test. [c] Chi-square test.

A stratified analysis of 70 vaccinated individuals showed no significant association between the sensitivity and the duration from the onset of symptoms to testing (Cramer's V = 0.084, $P = 0.955$; Table 4). Similarly, the stratified analysis of 45 individuals who used Abbott rapid antigen test and of 80 individuals whose PCR sample type was saliva showed no significant associations between the two (in the order: Cramer's V = 0.181, $P = 0.688$; Cramer's V = 0.087, $P = 0.895$).

DISCUSSION

Using 656 cases, we compared the rapid antigen and PCR test results for COVID-19 that were conducted on the same day among players and staff members of the Japan Professional Football League and clubs from January to March 2022, when the Omicron variant emerged, to determine the sensitivity and specificity of the rapid antigen test compared with the PCR test. We also investigated the relationship between the sensitivity and the duration from the onset of symptoms to testing, vaccination status, or test type.

The sensitivity was 0.63 (95% CI: 0.53–0.73) and specificity was 0.998 (95% CI: 0.995–1.000). The specificity was possibly an underestimate because there may have been fewer reports on the number of cases that were negative for both tests than the actual number. The sensitivity was not significantly associated with the duration from the onset of symptoms to testing. Consistent results were found in the stratified analysis of only those who were vaccinated, those whose kit manufacturer was Abbott, and those whose PCR sample type was saliva. Overall, the effect sizes were small (Cramer's $V < 0.2$). Furthermore, the sensitivity was not associated with vaccination status or test type (Cramer's V or $\varphi \leq 0.22$).

The results indicated that the sensitivity of the rapid antigen test compared to the results of the PCR test was independent of the duration from infection to testing or the presence or absence of symptom onset. This result was in contrast to that of a previous report (preprint) [6]: sensitivity of the rapid antigen test (Abbott or Quidel) compared with that of the PCR test (sample type: saliva) was 0.25 within 2 days from the first positive PCR test to the target testing and 0.9 since 3 days. The sensitivity

in our study was higher than the sensitivity of the previous study (i.e., 0.25 within 2 days from the first positive PCR test to the target testing). One possible explanation is that the players and staff members who participated in our study received lectures from their physicians on how to collect samples and that the tests were performed routinely, so that the samples were collected appropriately. The sensitivity of the rapid antigen tests may decrease when the tests are not performed according to the manufacturers' instructions for use [14]. Proper sample collection can lead to a high sensitivity.

The results of our study, which showed that the sensitivity of the rapid antigen test compared with the PCR test was 0.63 (95% CI: 0.53–0.73), may be used in combination with a model analysis to provide the fundamental knowledge required to establish a highly effective and efficient testing system. For example, a model analysis has estimated that the use of frequent rapid antigen testing is more effective than infrequent PCR testing in reducing the infection risk among populations such as professional sports players and staff members [15]. Under the assumption of an incubation period of 5 days, an R_0 of 4, and isolation with a test positive result, the infection risk (defined as "number of infected individuals remaining at the end of the 2-week isolation") among populations, in which a daily rapid antigen test with a sensitivity compared with a PCR test of 0.6 that was conducted for 2 weeks, was estimated to be as effective as when PCR testing was performed every 3 days [15]. Similarly, the sensitivity of 0.5 and 0.7 was equivalent to a PCR test being performed once every 4 days and every 2 days, respectively. Since the cost of the rapid antigen test is approximately one tenth that of the PCR test, the rapid antigen test can be performed more frequently than the PCR test assuming the same financial resources, and is therefore expected to be highly effective in controlling infection.

However, since the Omicron variant is more infectious than previous variants [16] and has a shorter incubation period [17], future testing strategies are expected to be combined with further model evaluations to match the characteristics of the Omicron variant.

Our study had some limitations. First, not all rapid antigen tests could be paired with a PCR test on the same date. Second, some of the cases in which both tests were negative may not have been reported to the Japan Professional Football League, which may have resulted in the underestimation of specificity, as described above. Third, the manufacturer of the test kits, and the samples used in the PCR tests, were based on the data provided by the clubs, and it was not possible to identify the manufacturer or sample types used by some participants. Therefore, we did not analyze the association between the sensitivity and the manufacturer or sample types. However, we confirmed that there was no association between the sensitivity and the duration from the onset of symptoms to testing by performing a stratified analysis of only those for whom the manufacturer was Abbott or the PCR sample type was saliva. Fourth, this study did not provide clinical diagnostic information on COVID-19. Therefore, it was not possible to assess the sensitivity of the rapid antigen test against the clinical diagnosis. In this regard, however, the PCR test is used world-wide as the gold standard to diagnose COVID-19, although the sensitivity of PCR against the clinical diagnosis was not 100% [18]. We therefore assessed the sensitivity of the rapid antigen test compared with the PCR test. Fifth, we could not obtain information on the participants' age, gender, presence or absence of underlying diseases, or history of COVID-19 infection. The Ct values for the PCR tests were also only available from some of the participants. Therefore, it was not possible to evaluate the association between the

sensitivity of these items. Since the sensitivity of the rapid antigen test varies depending on the Ct value in a wild-type strain [19], it may be useful to calculate the sensitivity of the rapid antigen test for the Omicron variant by stratified analysis using Ct values in a further study. Sixth, SARS-CoV-2 viruses were not sequenced to confirm them as the Omicron variant. However, since the Omicron variant was predominant in the period under study (98.92% [11]) as described above, the possibility of other variants was very low. Seventh, the participants of this study were professional sports players and staff members who had been lectured by their physicians about the testing procedures and who were tested on a regular basis frequency. Caution is therefore required in applying the findings of our study to populations that may not be accustomed to testing procedures and such sample collection. Despite such limitations, we analyzed the sensitivity and specificity of the rapid antigen test against the PCR test during the Omicron variant outbreak, and found that the sensitivity was independent of the duration from the onset of symptoms to testing.

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Contributors

M.M., H.S., T.I., M.K., W.N., T.Y., and S.I. contributed to the conception of the study. H.S. and T.I. contributed to data curation. M.M. contributed to formal analysis, methodology, and visualization. S.I. contributed to supervision and project administration. M.M. drafted the manuscript. H.S., T.I., M.K., W.N., T.Y., and S.I. reviewed and edited the manuscript.

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Competing interests

H.S. and T. I. received salaries from the Japan Professional Football League. W.N. and T.Y. have received financial support from the Japan Professional Football League, the Yomiuri Giants, Tokyo Yakult Swallows, the Japan Professional Basketball League, and the Kao Corporation in the context of measures at mass-gathering events. M.M., M.K., W.N, T.Y., and S.I. have attended the New Coronavirus Countermeasures Liaison Council jointly established by the Nippon Professional Baseball Organization and the Japan Professional Football League as experts without any reward. W.N. and T.Y. were/are advisors to the Japan National Stadium and Japan Professional Football League. The data used in this study were provided from the Japan Professional Football League. Otherwise, these institutions had no role in study design. The findings and conclusions of this article are solely the responsibility of the authors and do not represent the official views of any institution.

Data availability statement

We have included all the data produced in the present work in the manuscript. Note that the raw data used in the study were provided by the Japan Professional Football League, as described in this paper.

We are unable to attach all the raw data for each participant in this paper due to the ethical restrictions.

Notes

This article has already been registered for Preprints on medRxiv.

DOI is as follows: https://doi.org/10.1101/2022.06.13.22276325

(https://www.medrxiv.org/content/10.1101/2022.06.13.22276325v1).

Ethics approval

This study was conducted with the approval of the Ethics Review Committee of the Institute of Medical Science, University of Tokyo (approval number 2022-1-0421). Testing was not conducted originally for research purposes and the Japan Professional Football League does not have personal information relating to all results. Therefore, information about this study was disclosed on the websites of the Institute of Medical Science of the University of Tokyo and the Japan Professional Football League to provide participants with the opportunity to opt out of the study. The person in charge of each club also provided information about the study to potential participants (players and staff members).

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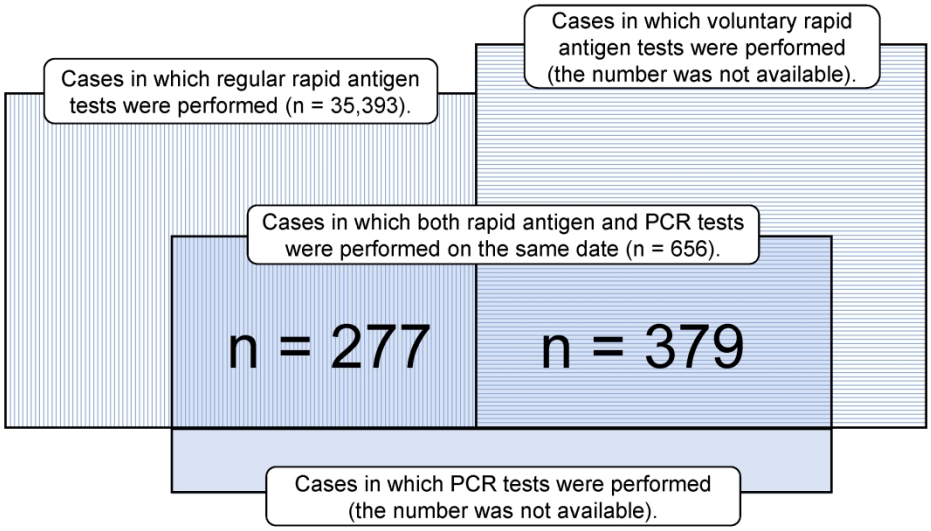
Figure caption

Figure 1. The number of the rapid antigen and polymerase chain reaction (PCR) tests during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs.



The number of the rapid antigen and polymerase chain reaction (PCR) tests during the Omicron variant outbreak among players and staff members of the Japan Professional Football League and clubs.

254x140mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2 [in the cleaned manuscript]
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-10
Bias	9	Describe any efforts to address potential sources of bias	6-10
Study size	10	Explain how the study size was arrived at	6-8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-11
		(*b*) Describe any methods used to examine subgroups and interactions	10-11
		(*c*) Explain how missing data were addressed	na
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	10-11
		(*e*) Describe any sensitivity analyses	11
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	na
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11-13

		(b) Indicate number of participants with missing data for each variable of interest	na
Outcome data	15*	Report numbers of outcome events or summary measures	11-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-13
		(*b*) Report category boundaries when continuous variables were categorized	11-13
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17-18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.